Skysong Innovations
Advancing the Arizona State University Knowledge Enterprise

1475 N. Scottsdale Road, Suite 200
Scottsdale, AZ 85287-3538
Phone: 480 884 1996 Fax: 480 884 1984

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Inventors

George (Bob) Pettit

Fiona Hogan

Steven Toms

Contact

Jovan Heusser
jovan.heusser@skysonginnovations.com

Auristatin Tyramine Phosphate Prodrugs and Aminoquinoline Derivatives

The remarkable anticancer properties of dolastatin 10, isolated from the sea hare (sea slug) Dolabella auricularia, have led to interest in closely related derivatives (auristatins) suitable for clinical trials. Most recently, such auristatins have been linked to antibodies for delivery. In many indications, however, it would be desirable to deliver such drugs without resort to conjugation.

Researchers at Arizona State University have developed prodrug forms of a novel auristatin tyramine derivative as phosphate salts, as well as auristatin quinoline modifications. These compounds exhibit superior inhibition of cancer cell growth. In addition, auristatin TP sodium salt is water soluble, and is thus expected to have greater bioavailability.

Existing auristatin drugs (e.g., SGN-35) are showing promise in clinical trials. The above novel compounds may have important advantages over such existing auristatin drugs and may prove to be important drugs for treating cancer.

Potential Applications

- Inhibiting cancer cell growth
- Treating many types of cancer

Benefits and Advantages

- Novel compounds displayed very strong cancer cell growth inhibition against a panel of murine and human cancer cell lines
- Auristatin TP sodium salt:
  - Water soluble
  - No need for conjugation to a macromolecule, such as an antibody, for delivery
  - Likely greater bioavailability than other forms of the drug
- Auristatins 2-AQ and 6-AQ
  - Aminoquinoline modifications of dolastatin 10
  - Various biological activities have been reported for simple derivatives of aminoquinolines, and these moieties are expected to confer distinct activity
  - Suitable for attachment to an antibodyFor more information about the inventor(s) and their research, please see

Dr. Pettit's departmental webpage